

### Remarks

Claims 99-201 are pending in this application. Claims 99-182, 194, 195, and 198-201 have been withdrawn as directed to a non-elected application.

In the Office Action mailed June 1, 2004, claims 183-193, 196, and 197 were rejected under 35 U.S.C. § 112, first paragraph, for lack of written description and under 35 U.S.C. § 112, second paragraph, for indefiniteness. Claims 183, 187-189, 191-193 and 196-197 were rejected under 35 USC § 103(a) for obviousness over Goldenberg in view of Barbet and Horowitz. Claim 190 was separately rejected as obvious over Goldenberg in view of Barbet and Horowitz. Claims 183-193, 196 and 197 also were rejected for obviousness-type double patenting over claims 1-9 of US Patent No. 6,387,350. The specific grounds for objection, and Applicants' response thereto, are set out in detail below.

#### Rejection under § 112, first paragraph

Claims 183-193, 196, and 197 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of written description. Specifically, the Examiner alleges that the specification fails to provide adequate support for the term "wherein said detection is performed without the use of a contrast agent or subtraction agent." Applicants respectfully traverse because the allegedly offending term is fully supported in the specification.

To satisfy the written description requirement, an applicant must convey to those skilled in the art that he or she was in possession of the invention as of the filing date. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). The PTO has the *initial burden* of presenting evidence or reasons why persons skilled in the art would not recognize a description of the invention in the disclosure, as defined by the claims. *In re Wertheim*, 541 F.2d 257, 263, 191 USPQ 90, 97 (CCPA 1976).

The Examiner acknowledges that the term "wherein said detection is performed without the use of a contrast agent or subtraction agent" is present in original claim 23 but asserts this "negative proviso" in claim 23 is directed to a different method than that recited in the instant claims, and that the specification lacks support with respect to the claimed methods that use a bispecific antibody that binds to an antigen produced or associated with a lesion, and to a hapten. Applicants respectfully note that the "negative proviso" also is present in original claims 36, 46,

and 90, and that this recurrent recitation indicates applicants' intention that each of the methods recited in the original claims could be carried out in the absence of a contrast or subtraction agent.

Nevertheless, without acquiescing in the propriety of the rejection, applicants have amended claim 183 to remove the term "wherein said detection is performed without the use of a contrast agent or subtraction agent," thereby mooting the rejection.

#### **Rejection under § 112, second paragraph**

Claims 183-193, 196, and 197 stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness. Specifically, the Examiner alleges that the "wherein said detection is performed without the use of a contrast agent or subtraction agent" is "confusing." The Examiner further alleges that claim 184 lacks antecedent basis in the related independent claim 183. Applicants respectfully traverse.

With respect to the terms "contrast agent" and "subtraction agent" these terms are defined in the cited Goldenberg reference (U.S. Patent No. 4,932,412) and are well known in the art. Nevertheless the amendment to claim 183 set forth above moots this rejection.

With respect to the alleged lack of antecedent basis for claim 184, the Examiner apparently misapprehends the rejected claim. Claim 184 adds an additional step to the methods of claim 183 ("[T]he method of claim 183, *further comprising* the step of....") and therefore no antecedent basis is required for this additional step. Withdrawal of the rejection respectfully is requested.

#### **Rejections under 35 USC § 103(a)**

Claims 183, 187-189, 191-193 and 196-197 are rejected under 35 USC § 103(a) for obviousness over Goldenberg in view of Barbet and Horowitz. Claim 190 is separately rejected as obvious over Goldenberg in view of Barbet and Horowitz. Specifically, the Examiner states that Goldenberg describes an intraoperative or endoscopic procedure using a bispecific labeled antibody fragment but fails to describe use of a bispecific antibody fragment where one arm binds a hapten, or the use of a radiolabeled hapten. Barbet is cited as teaching methods of radiodiagnosis or radiotherapy using bispecific antibodies where one arm binds a radioactive

happen. This rejection fails to describe the relevance of Horowitz and therefore applicants assume this is a clerical error. With respect to the rejection of claim 190, the alleged teachings of Goldenberg and Barbet are as described above but fail to describe methods of brachtherapy. Horowitz is cited as teaching that brachytherapy is a well known method of treating tumors using a catheter. Applicants respectfully traverse.

When combining references to make out a *prima facie* case of obviousness, the examiner is obliged to show by citation to specific evidence in the cited references that (i) there was a suggestion/motivation to make the combination and (ii) there was a reasonable expectation that the combination would succeed. Both the suggestion/motivation and reasonable expectation must be found within the prior art, and not be gleaned from applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991); *In re Dow Chemical Co.*, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988); *W.L. Gore v. Garlock, Inc.*, 220 USPQ 303, 312-13 (Fed. Cir. 1983) (holding that it is improper in combining references to hold against the inventor what is taught in the inventor's application); *see also* MPEP §§ 2142-43. Thus, the examiner must provide evidentiary support based upon the contents of the prior art to support all facets of the rejection, rather than just setting forth conclusory statements, subjective beliefs or unknown authority. *See In re Lee*, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002). In the present case the Examiner has failed to show either a motivation/suggestion to combine the cited references or a reasonable expectation that the combination would succeed for its intended purpose. Accordingly, withdrawal of the rejection respectfully is requested.

The entire basis for the rejection is set forth in one paragraph of the office action, bridging pages 4 and 5. In essence, the Examiner asserts that it would have been obvious to one of ordinary skill in the art to modify the methods of Goldenberg using the antibodies described by Barbet because "it is known" [sic] that methods of radiodiagnosis using site specific radiolabeled antibodies can be made "more effective" by using a two step approach as described by Barbet, and that one skilled in the art would have been motivated to use the Barbet antibodies to "improve the effectiveness" of the Goldenberg methods. This rationale falls far short of the specific evidence within the cited references that is required to support a rejection under § 103. Accordingly, the rejection is improper and should be withdrawn.

The rejection set forth in the office action is a classic "pick and choose" rejection where the Examiner finds the various aspects of the claimed invention in a variety of prior art references but fails to show why one of ordinary skill in the art would have been motivated to combine the cited references. Nothing in Goldenberg teaches or suggests that a two step approach using a bispecific antibody that binds to a target and to a hapten would be effective in operative, endoscopic, laparoscopic, intravascular catheter, or surgical procedures. Nothing in Barbet teaches or suggests that methods of administering a bispecific antibody and a radiolabeled hapten would be effective in operative, endoscopic, laparoscopic, intravascular catheter, or surgical procedures. The only motivation to combine these references is found in applicant's specification, and it is improper in combining references to hold against the inventor what is taught in the inventor's application. *Gore*, 220 USPQ at 312-13 (Fed. Cir. 1983).

Moreover, not only do the cited references lack any motivation or suggestion to combine the references, but nothing in the references would have provided one of ordinary skill in the art with a reasonable expectation that the combination would be successful for its intended purpose. In particular, nothing in Barbet suggests that the two step methods using bispecific antibodies would be useful or effective in close range methods such as those recited in the instant claims. Similarly, nothing in Goldenberg teaches or suggests that the methods described therein can be practiced using anything other than directly labeled antibodies, let alone that superior results might for some reason be obtained by using bispecific antibodies.

In sum, applicants respectfully submit that this rejection is based on an improper hindsight reconstruction of the instantly claimed invention. Nothing in the cited references would have suggested combining the references, nor suggested that the combination would be successful. Accordingly, withdrawal of the rejection respectfully is requested.

The rejection of claim 190 relies on the combination of Goldenberg and Barbet, which is improper for the reasons set forth above. Horowitz is merely cited for the proposition that brachytherapy is a known method of treating tumors using a catheter and fails to cure the problems with the primary references. Accordingly, withdrawal of the rejection of claim 190 also is requested.

**Obviousness-type double patenting**

Claims 183-193, 196 and 197 are rejected for obviousness-type double patenting over claims 1-9 of US Patent No. 6,387,350. Applicants respectfully request that this rejection be held in abeyance until the indication of allowable subject matter in the instant application, at which time applicants will consider the filing of a suitable terminal disclaimer.

### CONCLUSION


In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, Applicants authorize the Commissioner to charge any deficiency to Deposit Account No. 08-1641.


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Respectfully submitted,

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I hereby certify that this Amendment is being facsimile transmitted to the U.S. Patent and Trademark Office (Fax No. (703)872-9306) on November 1, 2004.

  
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